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Biography

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Abstract

The emergence of manipulation techniques that dampen, disassociate, erase, and replace unsavory episodic memories have given pause to even the most ardent proponents of the practice. Supporters of memory manipulation have since clarified that the interventions should be made available exclusively in extreme and limited-use cases. In light of the narrowing of this approach, the present essay examines the arguments in favor of limited-use memory manipulation (LUMM) for the two most commonly-cited circumstances in which the practice is claimed to be justified: post-traumatic stress disorder (PTSD) and substance addiction. After examining the neuroscience of PTSD and substance addition, the critical concepts of biomedicalization and the codification of new diseases, the myth of global autonomy loss, and the terminal normlessness of LUMM are explored to underscore the false hope of deliberate forgetting.

Keywords

Limited-Use Memory Manipulation, Post-Traumatic Stress Disorder, Substance Addiction, False Hope

1. The Case in Favor of LUMM for PTSD

Proponents of LUMM argue that is it morally reasonable, as a last resort, for individuals at risk of severe PTSD to be offered prophylaxis against the condition after enduring exceptionally traumatic and vastly disproportionate circumstances, such as the horrors of brutal rape or the recovery of fellow comrades' bodies (Donovan 2010). Inasmuch as death associated with war is considered morally acceptable in particular circumstances, and the risk of death in war is typically outweighed by any benefits to be gleaned, proponents suggest that helping those who executed a military agenda, risked death and dishonor, and subsequently suffer from a condition associated with their service should be considered an ethical obligation. If it is reasonable, on the one hand, to ask individuals to engage in life-threatening and emotionally distressing activities, then it seems wrong, on the other hand, to deny them therapeutic medications that may significantly reduce their considerable risk of developing PTSD. Moreover, proponents note that objections to the preventative use of beta-blocking pharmacologicals overlook ethical questions about post-trauma debriefing that, they maintain, has little to no effect

and, at worst, increases the risk of PTSD (Bryant 2002). As Wayne Hall and Adrian Carter (2007) maintain, when compared with countless hours of psychological intervention of uncertain efficacy, a seven-day course of a low-toxicity drug seems trivial.

1.1 The Neurobiology of PTSD

Psychological trauma often results from witnessing events that are perceived as life threatening or injurious to self or others (Sherin and Nemeroff 2011). Such experiences, which frequently evoke intense fear, horror, and helplessness, can lead to the development of PTSD. The condition was originally thought to represent a normative response (at the extreme end of the response continuum) to severe trauma or stress. However, it has become clear that the idiosyncratic response of an individual to trauma depends not only on stressor characteristics, but also on factors specific to the individual. For the majority of human beings, the psychological trauma induced by the experience of profound threat is acute and transient. Psychological trauma is typically characterized by phenomena that can be grouped into three domains: (i) reminders of exposure (including flashbacks, intrusive thoughts, and nightmares), (ii) activation (including hyperarousal, insomnia, agitation, irritability, impulsivity, and anger), and (iii) deactivation (including numbing, avoidance, withdrawal, confusion, derealization, dissociation, and depression). Self-limiting by definition, these reactions generally effect minimal impairment over time. For a (significant) minority of the population, however, the psychological trauma brought about by the experience of profound threat leads to a longer-term syndrome that has been defined, validated, and termed "PTSD" in the clinical literature. PTSD is accompanied by devastating functional impairment characterized by the presence of signs and symptoms in the three primary domains mentioned above (Sherin and Nemeroff 2011).

Contemporary neuroimaging has identified and confirmed characteristic changes in brain structure and function in individuals with PTSD (Sherin and Nemeroff 2011). Altered brain regions include the hippocampus, amygdala, anterior cingulate, insula, and orbitofrontal region. Together, these form a neural circuit that mediates adaptation to stress and fear conditioning. Changes in these circuits have been postulated to share a direct link to the development of PTSD. A hallmark feature of PTSD is reduced hippocampal volume. The hippocampus is implicated to control stress responses, declarative memory, and contextual aspects of fear conditioning. In fMRI studies, small hippocampal volumes were associated with trauma severity and memory impairments. The functional role of the amygdala, which mediates stress responses and emotional

learning, is also involved in the pathophysiology of PTSD. Given that increased amygdalar activity has been linked to genetic traits that moderate PTSD, increased amygdala activity may represent a neurobiological risk factor for developing PTSD. The medial prefrontal cortext (MPFC) comprises the anterior cingulate cortex (ACC), subcallosal cortex, and medial frontal gyrus. The medial PFC exerts inhibitory control over stress responses and emotional reactivity through its connections with the amygdala, and mediates extinction of conditioned fear through active inhibition of acquired fear responses. Individuals with PTSD exhibit decreased volumes of the frontal cortex, including reduced ACC volume, which has been similarly correlated with the severity of PTSD symptoms (Sherin and Nemeroff 2011).

The neurobiological concerns observed in individuals with PTSD are numerous and likely reflect an enduring dysregulation of multiple stress-mediating systems that occur as a result of psychological assault (Sherin and Nemeroff 2011). These pathophysiological disturbances occur in individuals with genetic, epigenetic, and experiential predispositions when exposed to extreme conditions, and presumably signify an indelible sensory imprint of maladaptively processed experience that effects an imbalanced degree of emotional import and releases (or restrains) behavioral reactions that aim to defend against future trauma via activation (or deactivation) in a losing effort to secure equilibrium. Hence, a lack of baseline cortisol at the time of psychological trauma may facilitate overactivation in the central corticotropin-releasing hormone - norepinephrine (CRH-NE) cascade, resulting in prolonged and enhanced stress responses. This increased stress responsiveness may be further accented by inadequate regulatory effects of gamma-aminobutyric acid (GABA), serotonin, and neuropeptide Y (NPY). Additionally, altered norepinephrine and stress hormone activity may be involved in processes of learning and extinction, both of which are abnormal in PTSD. For instance, norepinephrine enhances the encoding of fear memories and glucocorticoids block the retrieval of emotional memories. The constellation of elevated noradrenergic activity and relative hypocortisolism may lead to the encoding of traumatic memories and the lack of memory retrieval inhibition, both of which presumably trigger the re-experience of phenomena in PTSD (Sherin and Nemeroff 2011).

Additionally, a malfunctioning hippocampus may account for some cognitive symptoms of PTSD, including declarative memory deficits (Sherin and Nemeroff 2011). Since the hippocampus is critical for context conditioning, an impaired hippocampus may facilitate generalization of learned fear in contexts unrelated to previous traumatic exposure and so impair the ability to discern between safe and unsafe stimuli. In combination with exaggerated amygdalar responses associated with PTSD, a limited

capacity to discriminate threats may promote paranoia, hypervigilance, behavioral activation, exaggerated stress responses, and acquisition of additional fear associations. Disrupted PFC function may then serve to further exacerbate PTSD pathology as a result of deficient suppression of stress responses, fear associations, and extinction. To be sure, some neurobiological findings in patients with PTSD are controversial and require additional examination. Moreover, there are a number of understudied yet significant topics, including factors that impact resilience and vulnerability. For instance, stress-protective neurobiological factors such as activity in oxytocin and NPY-containing circuits could, in principle, be altered to promote resilience. Hence, there exists a general need for molecular biology to further explore PTSD to identify interactions between dispositional factors (both genetic and epigenetic) and trauma exposure to understand PTSD risk, gauge illness course, and predict treatment response. The effects of trauma on neurotrophic factors (in the hippocampus), neural plasticity (central nervous system [CNS]-wide), circuit remodeling (myelination patterns), and gene expression must be assessed in detail across illness duration. While difficult, such studies will necessitate accessing, assaying, and following populations at risk for exposure to trauma before exposure occurs (Sherin and Nemeroff 2011).

1.2 Beta-Adrenergic Receptor-Blocking Pharmacologicals as Treatment for PTSD

Propranolol, a beta-adrenergic receptor antagonist, is the primary pharmacological agent examined for treatment of PTSD (Donovan 2010).[1] This centrally acting, long chain, non-selective beta-blocker is highly protein bound and almost completely absorbed from the gastrointestinal tract with peak concentrations occurring in one to one and a half hours and a half life of approximately four hours (Strawn and Geracioti 2007). Preclinical studies have demonstrated that propranolol-induced beta-blockade in the rodent amygdala blocks memory reconsolidation, suggesting that treatment with propranolol following consolidation of traumatic events might interfere with the amygdalar retrieval of such events and thereby ameliorate unwanted symptoms associated with PTSD (Debiec and Ledoux 2004). Although direct antagonism of norepinephrine signaling may relieve PTSD symptoms, it is possible that propranolol exerts its therapeutic effect in PTSD by regulating substance P – a neuropeptide acting as both a neurotransmitter and neuromodulator system. Like norepinephrine, this pain-

1. While many beta-blocking drugs exist – including some that are more potent and prescribed more frequently than propranolol – the majority of research in this area has employed propranolol.

transmitting neuropeptide is tonically elevated and robustly secreted in response to acute psychological stress in individuals with PTSD. Preclinical data suggest that substance P can be attenuated by beta-antagonists (e.g., propranolol) but not alpha-1 and alpha-2 antagonists (e.g., prazosin). Interestingly, intrathecal administration of substance P to anesthetized rodents induces an increased heart rate that can be blocked by propranolol. Hence, it will be of significant future interest to determine if neurokinin-1 receptor antagonists (i.e., substance P antagonists) prove to be of clinical benefit to PTSD patients (Strawn and Geracioti 2007).

Current PTSD research has employed propranolol in three phases of memory: (i) acquisition, formation, and encoding, (ii) emotional response and consolidation, and (iii) retrieval and consolidation (Donovan 2010). If an event is anticipated as stressful, such as responding to a disaster, the administration of propranolol would influence formation, acquisition, and encoding. Administration immediately following a traumatic event – rape, for instance – would influence response and consolidation. Administration at a later point – for instance, during simulated arousal of PTSD in those who have been diagnosed – may influence recall, retrieval, and reconsolidation. The beta-adrenergic system is involved not only with response and memory formation, but also with the conditioning of emotional responses associated with memory. Hence, propranolol may both dampen memory formation and strip memories of their associated emotional responses. While this treatment has been termed "therapeutic forgetting" (Kolber 2007), it is not designed to make individuals forget physical experiences but rather dissociate emotions and fears from particular memories. Insofar as they slow heart rate and inhibit arterial vasoconstriction, beta-blockers have been administered for years as treatment for hypertension and cardiovascular disease. Although propranolol can interfere with hippocampal centers involved in memory storage – including dampening memory of trauma and enhancing memory of the events preceding it – there have been no reported cases of severe memory loss due to propranolol for cardiovascular conditions (Donovan 2010).

Michael Henry and colleagues (2007) cite multiple studies in which subjects were randomly given propranolol or placebo before exposure to both tragic and emotional stories and neutral and uneventful stories. When subjects were asked to recollect the stories, the placebo group recalled significantly more of the emotional story than the propranolol subjects. Further, there was no difference between the propranolol and placebo groups in recall of the neutral story. Christopher Reist and colleagues (2004) studied thirty-seven subjects who received oral doses of either forty milligrams of propranolol or placebo sixty to ninety minutes before stimulus exposure. The stimulus

was comprised of eleven slides that delineated a brief story. In the mundane version, a young boy witnessed a car accident en route to the hospital to visit his father. Upon arrival, the hospital staff was practicing an emergency drill. In the emotionally-charged version, the boy himself was injured in the car accident and sent to the hospital, where physicians worked to reattach his severed legs. Seven days post exposure, subjects were asked to recall the specific details of the slides they viewed and to take a seventy-six-question multiple-choice test that examined memory recollection. Reist and colleagues concluded that propranolol had a significant effect on attenuating memory in subjects who viewed the emotionally-laden story. Additionally, the heart rates of subjects who consumed propranolol were significantly lower than their placebo counterparts. If heart rate is considered a proxy for adrenergic activation, these results substantiate the likelihood that overactivation contributed to PTSD development through disrupted memory consolidation (Reist et al. 2004).

The foregoing data suggest that individuals in the fire, law enforcement, military, and rescue field may benefit from receiving propranolol prior to traumatic stimulus (Henry et al. 2007). However, it is more likely that propranolol would be used in hospital emergency departments to treat patients seeking medical attention shortly after assault, abuse, rape, molestation, or involvement in any sort of accident that may induce severe psychological trauma. Preliminary empirical studies in actual emergency situations have demonstrated the efficacy of propranolol in reducing PTSD symptoms. Roger Pitman and colleagues (2002) studied forty-one emergency department patients who experienced trauma likely to trigger PTSD. Within six hours of the traumatic occurrence, subjects were treated orally with forty milligrams of propranolol; the dose was repeated four times daily for ten days, with a nine-day taper period. After four weeks, symptoms of PTSD were detected in thirty percent of subjects given placebo and eighteen percent of subjects given propranolol. A similar clinical study by Guillaume Vaiva and colleagues (2003) of nineteen subjects demonstrated that thirty-seven and a half percent of those who refused propranolol had PTSD symptoms in contrast to nine percent of those who accepted it. Subjects were treated orally with forty milligrams of propranolol three times daily for seven days, with a twelve-day taper period. Prolonged adrenergic activation, as reflected by greater peritraumatic tachycardia, was prospectively shown to increase the risk for PTSD insofar as these states enhance fear conditioning mechanisms and the overconsolidation of memories related to traumatic events. This suggests that administering propranolol to young, healthy individuals with tachycardia is effective in mitigating PTSD symptoms and (possibly) preventing PTSD (Vaiva et al. 2003).

1.3 The Case in Favor of LUMM for PTSD

PTSD is a growing cause of human suffering that affects approximately one-third of all individuals exposed to major trauma (Hall and Carter 2007). Conventional psychological and pharmacological treatments for PTSD are often expensive, time-consuming, and of modest efficacy. On this basis, LUMM proponents argue that propranolol may be used, in extreme cases, to reduce the severity of psychological reactions to trauma and thereby reduce the risks of developing PTSD. While reasonable concerns have been raised about the use of drugs to alter memory, many (i) are based on wildly exaggerated and unrealistic scenarios that ignore the restricted and fleeting action of propranolol in affecting memory, (ii) underplay the utterly debilitating impact that PTSD has on those who suffer from it, and (iii) fail to acknowledge fully the extent to which other drugs – such as alcohol – are already used for this purpose. Anterograde amnesia is a well-known side effect of alcohol, as well as benzodiazepines available by prescription, such as Valium and Halcion, and illegally obtained benzodiazepines, such as Rophypnol. Unlike these drugs, propranolol has a retrograde amnesic effect, offering greater potential to ameliorate traumatic memories from the recent past (Kolber 2006). Henry and colleagues offer a scathing critique of the ethical concerns forwarded by the 2003 President's Council on Bioethics (PCB) about the prophylactic and dampening use of propranolol. The authors comment that the PCB's concerns involve a series of speculative harms – for instance, that criminals may consume beta-blockers to reduce painful memories of their crimes – that fail to provide concrete reasons to oppose trials to assess the safety and effectiveness of propranolol. Moreover, the PCB also fails, in their judgment, to make a persuasive case for proscribing the clinical use of propranolol if clinical trials indicate its effectiveness (Henry et al. 2007).

Wayne Hall and Adrian Carter (2007) expand the arguments of Henry and colleagues (2007) to articulate more broadly what is at stake, thereby forwarding the strongest (available) case in favor of LUMM for PTSD. The authors offer a consequentialist argument in favor of using propranolol – namely, that it may be employed to reduce the need for PTSD sufferers to use a more hazardous drug (e.g., alcohol) to treat their symptoms. In high doses, alcohol reduces anxiety and recall of emotionally traumatic memories, but chronic use for these purposes can quickly lead to dependence, a disorder that significantly reduces the chance of recovering from PTSD and has enormous health consequences, both individually and socially (Hall and Carter 2007). Following Henry and colleagues, the authors similarly reject the argument of the 2003 PCB that propranolol may be used by criminals to reduce regretful memories of their crimes, arguing instead that psychopaths cannot express interest in reducing the sting of such memories insofar

as they do not possess the emotional capacity for regret. Nonetheless, in the unlikely event that criminals used propranolol to numb their conscience, a positive outcome might include reduced alcohol abuse,[2] improved public order, and reduced burden on the families of criminals. Hall and Carter further suggest that concerns about propranolol being used by the military to prevent soldiers from developing painful memories of war crimes and atrocities do not reflect the pharmacological properties of propranolol, which serves to attenuate reactions to trauma rather than procure global amnesia of events and conscience. Somewhat ironically, they mention that atrocities such as those at Srebrenica, Vietnam, and in World War II did not depend on the use of beta-adrenergic antagonists,[3] suggesting that the psychology of war appears sufficient to account for such acts attracting strong and justified societal opprobrium in the unlikely event that perpetrators of atrocities use propranolol for these means (Hall and Carter 2007).

In response to the medico-legal argument that damages payouts may be reduced by the effects of propranolol, Hall and Carter comment that this merely signifies the perverse incentives in the legal system rather than a compelling argument against the use of propranolol by victims of traumatic crimes to reduce the severity of PTSD (Hall and Carter 2007). This concern also seems exaggerated, they note, inasmuch as criminal actions that traumatize can be corroborated in ways that do not depend on the memory of the victim or the severity of the PTSD symptoms subsequently developed. For instance, no legal system would acquit a rapist on grounds that the victim did not develop PTSD. Nevertheless, some studies suggest that propranolol may actually improve recall of memories that are impaired by trauma (Strange et al. 2003). Further, Hall and Carter remark that bioethicists who object to the preventative use of propranolol overlook moral questions about the genuine efficacy of post-trauma debriefing, which is purported to reduce the risk of PTSD. According to Richard Bryant, contemporary evidence suggests that, at best, debriefing has no effect and, at worst, increases the risk of PTSD (Bryant 2002). Compared to countless hours of psychological intervention of uncertain efficacy, the authors argue that a seven-day course of a low-toxicity drug seems trivial. Moreover, the use of propranolol to prevent the consolidation of traumatic episodic memories seems a risk worth taking in order to avoid a thirty-three percent chance of spending months undergoing psychotherapy and pharmacotherapy to treat

2. Alcohol is the overwhelming drug of choice for criminal offenders.

3. Ironically, this point may be used a foundation on which their argument may be refuted.

PTSD and the common complications of alcohol and other drug dependence (Hall and Carter 2007).

While Hall and Carter (2007) sympathize with the concerns of Henry and colleagues (2007) regarding the potential for over-promotion of drugs to treat PTSD, they make two observational points in reply. First, they argue that propranolol is already off patent, which makes it exceedingly unlikely to be promoted by any drug company. Second, they argue that while it is plausible that the production of new drugs with similar effects may be promoted in this way in the United States – where direct-to-consumer advertising of pharmaceuticals is allowed and there are few regulatory limits to prevent superfluous promotion – this possibility simply denotes the need for improved regulation of the pharmaceutical industry rather than a robust argument against the use of propranolol per se. In conclusion, they reiterate that most of the commonly raised ethical objections to the use of memory dampening drugs, including propranolol, overstate the possible negative consequences of its use and run the risk of hindering a promising advance in the prevention of PTSD that may significantly reduce the need for PTSD suffers to turn to more harmful drugs, such as alcohol. Moreover, the authors reinforce that conventional arguments against the use of propranolol fail to provide cogent reasons for either preventing a trial of its safety and efficacy or for preventing its clinical use once proven to be safe and effective. For Hall and Carter, then, the criticisms of the PCB should be recognized only as a form of scare-mongering: a hazard of bioethical analyses that is the product of "worst-casing" the potential harms of new biotechnologies, often as a result of exaggerating their effectiveness (Hall and Carter 2007).

2. The Case in Favor of LUMM for Substance Addiction

Proponents of LUMM argue that it is morally permissible, as a last resort, for substance addicts whose psychosocial condition poses a disproportionate and immediate threat to their overall health, well-being, and safety to be offered relief in the form of surgical or psychological memory editing. Impaired control over voluntary behavior is a marked feature in emerging neurobiological explanations of substance addiction, in clinical and diagnostic accounts, and in debates about addiction nosology (Wild et al. 2012). Hence, drug cravings can manifest as such irresistible and powerful psychological forces that someone with an addiction is not capable, at certain times, of acting fully autonomously when the decision involves denying the persistence of cravings. An addict might be excessively subservient to the individual who supplies him with drugs, or with money for drugs, and therefore have his autonomy compromised by the rule of another.

However, if the addict's autonomy is compromised in this way, it marks a consequence of an initial loss of autonomy that is characteristic of addiction (Wild et al. 2012). It follows, therefore, that such a loss of autonomy undercuts the addict's ability to pursue his own goals (Levy 2012).

2.1 The Neurobiology of Substance Addiction

Communication in the brain is facilitated by neurotransmitters that are released from neurons at synapses where they interact as bonds with protein complexes, called receptors, on the surface of other cells, predominantly at the postsynaptic membrane (Duncan and Lawrence 2012). The binding of a neurotransmitter to a receptor transduces a chemical signal that transfers activity-dependent information. The neurotransmitters can either be taken back up by the cell for future use by transporters or degraded and removed from the system. In the brain, pathways are complex integrative systems that contain numerous neurons or nuclei that relay information throughout a circuit and can be acted upon by other neurotransmitter systems that also integrate with that region. While addictive substances have diverse pharmacological profiles, their acute actions converge primarily on the mesocorticolimbic dopaminergic system. This pathway originates in the ventral tegmental area (VTA) and projects to the nucleus accumbens (NAc), striatum, forebrain, and PFC. The PFC coordinates cognitive processes and actions aimed at an internal goal, while the NAc is believed to integrate information, effect an appropriate response, and control the motivational value of stimuli and reward enforcement. Immediately after initial exposure to a drug, extracellular levels of accumbal dopamine increase. Some enhance dopamine release from the presynaptic terminals as a consequence of increased neuronal activity in the VTA (e.g., alcohol, nicotine, opiates, and cannabis) while others inhibit the presynaptic uptake by the dopamine transporter in the NAc (e.g., cocaine and amphetamines). Addictive substances produce a larger dopamine release that is maintained for longer than that of natural rewards. If exposure to the drug persists, there may be a loss of homeostatic regulation: a progressive increase in basal levels of dopamine is accompanied by a reduction in the lesser response to the drug, resulting in the appearance of tolerance to the drug (Duncan and Lawrence 2012).

During acute withdrawal, dopamine rebounds to below basal levels so re-exposure to the drug or a drug-related cue is often sufficient to increase dopamine again (Duncan and Lawrence 2012). This dopamine response has been hypothesized to contribute to addictive relapse, working on serotonergic, noradrenic, glutamatergic, and GABAergic systems. While dopamine release may modulate the acute rewarding effects of an

addictive substance, it does not solely mediate drug-seeking behaviors and persistent drug taking. Exposure to addictive drugs can have either a direct or indirect effect on numerous neurotransmitter systems. Unlike dopamine, which facilitates the response to initial drug use, these additional neurotransmitter systems play a greater role in mediating persistent drug use, contributing to the inability to terminate drug use and the likelihood of relapse after a period of abstinence. Glutamatergic inputs from the PFC, amygdala, hippocampus, and other brain regions modulate activity in the NAc either directly or indirectly by their influence on the VTA. Like to dopamine, initial exposure to a psychostimulant increases extracellular levels of glutamate in the NAc, PFC, and, to a lesser extent, the VTA. Unlike dopamine, however, this response increases the sensitivity of the receptors that bind glutamate to the effects of subsequent exposures to lower doses of the particular drug. This leads to reduced extracellular glutamate levels and, hence, decreased glutamate-driven activity over time. Upon re-exposure to the drug or drug-associated cue, there is enhanced synaptic glutamate release that drives continued drug-seeking behaviors. Such dysregulation of the glutamatergic system is sufficient to alter drug-induced behaviors, even in light of normal dopaminergic responses procured in the NAc (Duncan and Lawrence 2012).

Imbalance in the glutamatergic regulation of corticostriatal transmission has been termed the "glutamate hypothesis" of addiction, which suggests its cardinal role in mediating relapse (Duncan and Lawrence 2012). This hypothesis is supported by studies demonstrating that the reinstatement of drug-seeking behaviors can be prevented using the procysteine drug N-acetylcysteine (NAC) (Reichel et al. 2011). NAC increases glutathione synthesis, which restores glutamatergic signaling. Treatment with NAC is also able to restore prefrontal-driven long-term potentiation and long-term depression in the NAc, which are typically impaired during acute withdrawal. The therapeutic potential of NAC has now been trialed in preclinical human studies, where it has successfully reduced the desire to use drugs of abuse (Gray et al. 2010). Astrocytes express the sodium-dependent GLT1, which is responsible for removing over ninety percent of glutamate from the extracellular space. Overexpression of GLT1 in the PFC and the NAc during extinction training is sufficient to inhibit cue-induced reinstatement to drug self-administration by suppressing the excess extracellular glutamate that normally occurs upon re-exposure to a drug. Beyond relapse, imbalances in glutamatergic transmission have been hypothesized to mediate responses to drugs including self-administration, reward learning, extinction, and behavioral sensitization that, in animal subjects, is manifested by increased psychomotor activity. In the NAc, the modulation of glutamatergic inputs onto medium spiny GABAergic neurons expressing D_1 dopamine

receptors play a vital role in the development of sensitization to drugs. Thus, an allostatic shift – which marks an adaptive effort in a regulatory system in response to a chronic deviation from "normal," thereby establishing a new set-point – toward augmented glutamatergic function may contribute to the transition from controlled drug use to a compulsive and uncontrolled drug-dependent state and the high incidence of relapse (Duncan and Lawrence 2012).

There are vast numbers of neuropeptides and corresponding receptors present in pathways that mediate addiction. The role of corticotropin-releasing factor (CRF) is highlighted as an example of the intricate part that neuropeptides play in mediating addictive behaviors (Duncan and Lawrence 2012). Stress, either in the environment or due to substance withdrawal, can induce drug craving, which leads to relapse. The system mediating stress responses incorporates the HPA and extrahypothalamic regions (such as the extended amygdala). CRF is a neuropeptide that is responsible for activating the HPA, where it plays a mediating role in hormonal, autonomic, emotional, and behavioral responses to stress. Initial exposure to a drug engages the HPA, but this response becomes blunted with repeated exposures via feedback systems in response to circulating hormones. CFR-mediated actions on addictive behaviors depend on their interplay at extrahypothalamic sites. These extrahypothalamic regions become sensitized to CRF after repeated exposure to substance abuse. During withdrawal, these regions become engaged and hyperactive, thereby increasing local CRF levels and perpetuating negative states of stress. While stress is sufficient to increase CRF levels in the VTA, it is neuroadaptive changes induced by prior drug abuse that enable the CRF to control local glutamate release, subsequently activating the dopaminergic system and perpetuating stress-induced relapse to drug-seeking behaviors. There remains debate about the particular sites of action for CRF beyond the HPA. CRF acts primarily through either CRF1 or CRF2 receptors, both of which are widely distributed throughout the brain. CRF1 receptors have been hypothesized to play a significant role in addiction sensitization and relapse. One study suggests that a CRF1 receptor antagonist was sufficient to decrease the reinstatement of drug-seeking behavior in a previously abstinent rodent that was given cocaine (Przegaliński et al. 2005), although more recent studies support the role of CRF1 receptors in active drug taking (Specio et al. 2008). Chronic inhibition of CRF1 receptors is also sufficient to induce long-term adaptations to the dopaminergic system, including reducing the density of dopaminergic projections in the striatum and increasing dopamine receptor expression in a subtype-specific manner. Comparatively, stress-induced reinstatement to addictive substances can be prevented by infusions of a CRF2 receptor antagonist into the VTA. This most likely indicates inhibition of glutamate and dopamine

release, even through CRF1 receptors are dominant in this region (Duncan and Lawrence 2012).

2.2 Deep Brain Stimulation and False Memory Creation as Treatments for Substance Addiction

DBS is a surgical procedure in which an electrode is implanted in one or more specific areas of the brain and high-frequency electrical stimulation (130-180 Hz) is delivered to target sites (Henderson et al. 2010). This procedure ameliorates symptoms associated with movement disorders and has been moderately effective for intractable pain. The use of DBS is now being extended to include a variety of psychiatric disorders, including obsessive-compulsive disorder and depression. The NAc has a pivotal role in the pathogenesis of substance addiction and is an important element in the mesocorticolimbic reward circuit. As such, it is immediately involved in establishing the reward of drugs of abuse. Numerous researchers now contend that dysregulation of the neurophysiological processes involved in creating the quality or intensity of rewarding experiences contributes to addiction. For these reasons, the NAc is an ideal target for DBS, and early studies have shown promise. DBS in the NAc has selectively blocked the return of psychostimulant use and reduced morphine-induced place preference. For one individual who received DBS to alleviate anxiety and depression, stimulation in the NAc had the unintended consequence of improving the individual's comorbid alcohol dependence (Kuhn et al. 2007). Data from a subsequent animal study indicated brief periods of DBS in either the core or shell of the NAc reduced alcohol consumption in rats trained to drink alcohol. The purpose of the study was to indicate the potential of DBS to reduce human alcohol preference and its deprivation effect. This occurred with no sucrose fading or any other behavioral modification to induce alcohol consumption. Hence, DBS may serve as a solitary or adjunctive therapy for individuals resistant to current treatments for substance addiction (Henderson et al. 2010).

Drug aversion therapies have historically included electroconvulsive techniques (in which an electric shock is used as a negative stimulus pairing when the individual is engaged in thoughts, urges, or behaviors related to the addictive substance), satiation (a technique primarily used with cigarette smokers whereby individuals smoke a large number of cigarettes in a short period of time to induce nicotine toxicity), and chemical aversant pairings (in which a repugnant smell or taste, or even an intravenous pharmacological agent, is administered to induce sickness) (Clifasefi 2013). Ethical concerns, as well as a lack of controlled scientific studies in these areas, have led to the

demise of conventional aversion techniques. Nevertheless, some drug programs still integrate aversion therapy in their methodologies. Current (acceptable) pharmacological treatments for substance addiction include the administration of inhibitory agents (e.g., Disulfiram) that act by blocking the breakdown of acetaldehyde, the chemical believed to contribute to withdrawal symptoms. The interaction of Disulfiram with any amount of an addictive substance enhances unpleasant physical symptoms – including throbbing headache, nausea, vomiting, and weakness – deterring the individual from subsequent use. Today, an alternate approach to curbing substance addiction can be found in the pseudomemory literature. Over the past twenty years, the literature on FMC has suggested the possibility of having individuals imagine an event that purportedly happened in their past through innocuous suggestions and eventually believing (with confidence) that the event occurred (Clifasefi et al. 2013).

Results from a handful of FMC studies have indicated that adopting false memories as part of one's personal autobiography can affect an individual's current and future preferences related to those memories (Clifasefi et al. 2013). These findings demonstrate promise for related behaviors that carry devastating health risks, such as substance addiction. To date, only one study has experimentally examined whether early substance-related memories would be prone to memory manipulation. Seema Clifasefi and colleagues (2013) suggested to their trial participants that they had become sick during their early teenage years (prior to age sixteen) after exposure to a particular type of drug, and examined whether they would (i) increase their confidence that the suggested event occurred and, if so, (ii) demonstrate a decreased preference for the specific drug mentioned. Overall, experimental participants who received a false substance-related suggestion exhibited a significant increase in confidence compared to controls that the event did occur. More significantly, individuals who received a false suggestion that they had become sick from a particular drug showed a trend toward diminished preference for the drug in a follow-up preference rating task. Taken together, false memories about becoming sick from a specific drug in one's young adulthood appears to have implications for an individual's current and future associations with that drug. The findings of Clifasefi and colleagues are consistent with the drug expectancy literature, which indicates that positive drug expectancies are associated with increased and risky drug-related behavior, whereas negative drug expectancies are associated with decreased drug-related behavior (Clifasefi et al. 2013).

To be sure, the 2013 study by Clifasefi and colleagues is not without limitations, five of which are particularly worthy of note. First, it is important to illuminate that only 19.6 percent of experimental subjects developed a memory or belief that the drug-

related memory occurred. Second, the fact that disparities existed between experimental and control participants at baseline vis-à-vis drug preference does not preclude the possibility that preference findings are due to regression to the mean. Third, the data suggests that those who reported a younger first drug-related experience were more likely to adopt the false suggestion. Fourth, it can be argued that insofar as early onset drug users are known to be at higher risk for subsequent problems, these individuals may ultimately be remembering true events from their past. Finally, another argument can be made about early age-of-onset drug use – namely, that these individuals might show different cognitive vulnerabilities than their late(r) age-of-onset counterparts. These limitations notwithstanding, the foregoing data suggests that, in some cases, preference for a particular drug may be altered via FMC. Thus, drug-related memories evoked about one's past (whether true or false) have particular consequences for one's current thoughts, preferences, and, ultimately, drug-seeking behavior. Moreover, the finding that individuals who reported a younger first drug experience were more likely to adopt the false suggestion may be of particular interest to addiction researchers given what is known about the connections between age of first drug experience and subsequent development of drug dependence. Ralph Hingson and colleagues (2006), for instance, have demonstrated that individuals who were exposed to an addictive substance prior to age fourteen are approximately five times more likely to experience dependence compared to those exposed at age twenty-one or older. In a similar vein, the study of Clifasefi and colleagues highlights additional cognitive characteristics of individuals who may be at risk for developing drug problems (Clifasefi et al. 2013).

2.3 The Case in Favor of LUMM for Substance Addiction

Addictive behaviors clearly undermine individual and population health and exact a significant economic cost on global societies (Wild et al. 2012). Clinicians, researchers, policy makers, and society at large are therefore eager to implement effective policies and programs to reduce the medical and economic burdens of addiction. Treatment is one important response to these burdens. Addiction treatment programs have traditionally engendered the view that patients are sufficiently impaired and concerned by their addictions to seek help voluntarily. However, the case-mix has shifted dramatically over time, and mandatory treatment pathways are becoming increasingly entrenched in addiction treatment programs and policies around the world. These pathways include legal mandates from the criminal justice system, formal mandates from employers and social assistance agencies, and informal mandates (e.g., threats, ultimatums,

interventions, etc.) issued by family and friends, all compelling individuals with addiction to seek treatment. Mandated treatment policies and programs have been viewed as cost-effective and rehabilitative adjuncts to voluntary treatment and, on this basis, justifiable public health measures similar to seatbelt laws or mass immunization programs. The rationale for mandatory addiction treatment has recently been broadened to underscore findings from neuroscience research. Evidence of impairment in decision making and behavioral control in individuals with histories of substance abuse has been used to argue that individuals with such neurocognitive affliction are not capable of informed consent. Some scholars have expanded this argument by proposing that mandated addiction treatment should be used to restore patient autonomy and, to this end, can be justified according to a fundamentally humanitarian moral calculus (Wild et al. 2012).

Impaired control over voluntary behavior is a marked feature in emerging neurobiological explanations of substance addiction, in clinical and diagnostic accounts, and in debates about addiction nosology (Wild et al. 2012). There is growing evidence that chronic, sustained drug abuse is associated with neurocognitive changes and deficits, as revealed by neuroimaging studies (Bolla et al. 2003) and neuropsychological testing (Ersche and Sahakian 2007). Several studies propose that chronic exposure to drugs sets in motion neurobiological processes that result in overvaluing the reinforcing properties of a substance or behavior and an undervaluing of natural reinforcers (e.g., maintaining relationships, going to work, etc.) (Goldstein and Volkow 2002). These processes are associated with impaired voluntary control over one's behavior. Similarly, individuals experiencing addiction have neurological impairments that weaken their ability to make voluntary decisions in service of long-term outcomes. Despite cautionary assertions concerning the difficulty of making substantive generalizations or conclusions about the neuropsychological and neurobiological correlates of chronic drug use – due largely to the fact that findings are not always consistent in the nature or extent of deficits observed – results from neuroscientific studies have been used to argue that treatment is able to restore free will (Caplan 2008). This suggests that drug cravings can manifest as such irresistible and powerful psychological forces that someone with an addiction is not capable, at certain times, of acting fully autonomously when the decision involves denying the persistence of cravings (Wild et al. 2012).

Autonomy is a term with multiple meanings. In its maximal sense, autonomy means that human beings possess only the desires and beliefs they want to have and make choices uninfluenced by any factor they have not endorsed (Levy 2012). Certainly, if addiction threatens autonomy (as it seems to do), then it must be some less extravagant notion of autonomy that it undermines. In a minimal sense, autonomy is simply self-

government. Just as autonomous nations are able to make major decisions of internal and external policy without undue interference from foreign powers, so autonomous persons are capable of governing themselves by setting their own short- and long-term ends and choosing the best means of achieving them. One obvious situation in which autonomy is compromised or lost is when the self is ruled by another. In the political domain, the loss of autonomy is almost exclusively described this way. The same kind of phenomenon can occur, more or less dramatically, in the substance addict as well. A slave, for instance, whose life is entirely in the hands of another, is a dramatic example of this phenomenon, while a dispositionally subservient person might represent a less dramatic instance of this partial loss of autonomy. An addict might be excessively subservient to the individual who supplies him with drugs, or with money for drugs, and therefore have his autonomy compromised by the rule of another. However, if the addict's autonomy is compromised in this way, it marks a consequence of an initial loss of autonomy that is characteristic of addiction. This initial loss of autonomy has left the addict vulnerable to this subservience, since it is the addiction that gives the individual who controls him undue influence (Levy 2012).

There need not be another party exercising undue influence over the addict to experience a weakening of autonomy. The individual who is able to supply his habit is unlikely to be at the control of another as the consequence of addiction (Levy 2012). It is sometimes postulated that addicts are controlled by the drugs they abuse. Carl Elliot (2002), for instance, writes that the addict must go where addiction leads, because the addiction "holds the leash" (p. 48). Elliot's imagery is, of course, a metaphor: an addiction cannot hold a leash, is not an agent, and has no desires or goals of its own. If addiction involves the loss of autonomy, then it must somehow undercut the addict's ability to pursue his own goals. Elliott's claim that addicts are in thrall to their addiction echoes a long tradition of theorizing about addiction – namely, that addiction exercises complete control over drug-seeking and consuming behavior – found in the writings of philosophers, psychologists, and clinicians. For Louis Charland (2002), for instance, the addicted brain "has almost literally been hijacked by the drug" (p. 43); for Alan Leshner (1999), the initially voluntary behavior of drug-taking gradually transforms into involuntary drug-taking to the point where behavior is subsequently driven by compulsive cravings for the drug; and for Harry Frankfurt (1971), unwilling addicts struggle against their desires to no avail insofar as they are always "helplessly violated by their own desires" (p. 12). For these authors, addiction is compulsive, which is to say that addicts are forced to act as they do by virtue of an irresistible desire. Desires are irresistible when they become powerful enough to overwhelm an individual's capacity to overcome

or circumvent them. Thus, addiction is compulsive inasmuch as it produces desires that are so powerful that an addict cannot resist them (Levy 2012). This conception of how addiction functions dates back (at least) to William James (1890), who commented that "'if a bottle of brandy stood at one hand and the pit of hell yawned at the other, and I were convinced that I should be pushed in as sure as I took one glass, I could not refrain'" (ch. XXVI).

3. The Neuroethical Astigmatism of LUMM

Beta-blocking pharmacologicals, DBS, and FMC techniques used to block (i.e., blunt or dampen) or reverse (i.e., erase) the cognitive processes through which non-conscious recollections of past events deemed pathological and found to exacerbate PTSD and substance addiction are currently offered as treatments for specific diseases of mentality. Intended as prudent therapies, these treatments are widely experimental in the context of targeted manipulation and therefore transcend the respective purposes for which they were originally designed. Due to the experimental nature of their implementation, the long-term effects of their novel application are widely unknown. While the potentially harmful neurocognitive and more general biological effects already suggest their restriction from general use, this essay contends, for reasons beyond these implications, that even the most limited forms of neurocognitive manipulation cannot be justified as a morally licit biomedical practice, and that arguments in its favor are acutely neuroethically astigmatic.

3.1 The Astigmatism of LUMM for PTSD: Biomedicalization and the Codification of New Diseases

The primary neuroethical astigmatism of LUMM as a treatment for PTSD concerns the potential for unsavory memories to become medicalized and subsequently codified as a new disease category. A lingering effect of contemporary biomedical technologies is the medicalization of what has heretofore been considered "normal" states of being (Henry et al. 2007). Sociologists in the 1970s and 1980s defined medicalization as descriptive of at least two processes: first, placing what had previously been considered "normal" behavior under the medical gaze (Parsons 1979), and second, taking something deemed by society as pathological and placing it under the jurisdiction of medicine (Conrad and Schneider 1980). In recent years, new processes of biomedicalization have expanded the diagnostic conditions of illness to include more symptoms and greater numbers of individuals. This expansion is exemplified by cases of clinical depression and bipolar disorder, and it is

particularly evident in the extension of attention deficit hyperactivity disorder (ADHD) to include greater numbers of children and a growing adult population. The expansion of diagnoses is encouraged and promoted by pharmaceutical companies that produce drugs to treat disorders with the intention of codifying new disease categories. In turn, pharmaceutical companies sponsor disease awareness campaigns, advertise prescription drugs directly to consumers, and target clinicians at educational conferences and in medical offices to encourage them to prescribe their drugs. Sometimes referred to as "disease mongering" (Moynihan and Henry 2006), this newer process of medicalization allows pharmaceutical companies to capitalize on human suffering and exploit insecurities and unhappiness in order to increase drug sales (Henry et al. 2007).

Propranolol in particular seems especially ripe for pharmaceutical rebranding (Henry et al. 2007). A pharmaceutical company that wishes to manufacture and market a newer beta-blocker for the treatment of PTSD need only slightly alter its chemical composition to obtain a new patent and market the drug under a new name. It might, for example, promise fewer side effects, or longer-lasting effects than generic propranolol. The company responsible would then be able to brand the "new" (and likely more expensive) drug and market it with a new patent for the "new" ability to prevent PTSD. Granted this, various scenarios become possible. For instance, patients would be made aware of and offered the drug in the aftermath of a traumatic event. To sell more drugs, the company would specify a range of traumatic events for which its drug should be prescribed: rape, violent crimes, death of a loved one, and the like. Here, medicalization processes come into play. Trauma – its conception, parameters, and definition – is equal parts cultural and social, not medical. Yet the definition of trauma would be codified by the FDA through its indications for use of the new drug, and the pharmaceutical company that manufactures it may continually broaden the scope of trauma in order to sell more of its product. Take, for example, a drug advertisement in which an individual is encouraged to ingest propranolol following an embarrassing or humiliating experience at the office. This quixotic yet sobering example provides a substantive reason to be concerned that a private company seeking to sell more drugs will promote an expanded set of PTSD causes, altering both a sense of the illness and interpretations of the experiences that may cause it (Henry et al. 2007).

Moreover, the foregoing concern seems particularly acute in terms of employing the new drug as a prophylactic to trauma. Although the PCB (2003) has focused chiefly on the preventative uses of propranolol for military or emergency rescue teams, the company producing a new drug for PTSD would presumably attempt to market directly to consumers (Henry et al. 2007). Assuming the FDA approves the drug for this use,

questions are inevitably raised over the breadth and depth of traumas for which the new drug is appropriate. This essentially social question would then become defined primarily by the pharmaceutical company. If the new drug is marketed as prophylactic, it would be advertised to consumers who may be exposed to trauma in the near future. It may eventually become tempting for all individuals to have the new drug on hand for consumption before or after trauma, idiosyncratically defined. Falling in line with methylphenidate for ADHD and selective serotonin reuptake inhibitors for depression diagnoses, propranolol may be positioned as another catalyst of "diagnostic bracket creep" (Kramer 1993, 15), in which the availability of a new drug encourages the expansion of a diagnostic category. This is complicated further by the added nebulous category of "prevention" rather than treatment where the potential for expansion is even greater. If modern history has demonstrated anything, it is that scientific breakthroughs are often double-edged swords. However, if the PCB's language of "evildoers" and "pain" that is "deserved" has resonance at all in high political circles, it has little utility in the scientific and rational evaluation of new medical technologies and their potential dangers (Henry et al. 2007).

In addition to ethical qualms about biomedicalization and the codification of new diseases is the issue of capacity and, thus, informed consent (Henry et al. 2007). It is hardly controversial to question the capacity of research subjects or medical patients to give informed consent in the immediate aftermath of severe psychic trauma. While victims of rape and witnesses to murder are generally assumed to have decisional capacity to accept diagnostic and forensic tests (as well as psychotherapeutic and psychopharmacologic interventions), the use of propranolol as a targeted method of manipulation would require healthcare professionals to accept a lower threshold of capacity. However, researchers or clinicians utilizing this method must take decisional capacity seriously if they wish to maintain minimal treatment standards. If an individual is judged to be devoid of the ability to understand, evaluate, and reason about relevant information (whatever the cause), then this precludes the individual from free participation in PTSD research. No risk, however small, should be imposed in these circumstances. The prevention of PTSD with propranolol does not constitute a medical emergency as it has been traditionally defined – that is, when the consequence of withholding a particular treatment is that death will ensue, or the patient's health will be substantially compromised. If, on the contrary, the prevention of PTSD were to become understood as an emergent circumstance (as defined above), then patients with capacity who refuse propranolol or whose surrogates consent for them would be physically forced or psychologically coerced into taking the drug against their will. In addition to this being

an unjustifiable form of paternalism, such forceful and counterintuitive behavior would likely place an additional psychic burden on an already vulnerable person (Henry et al. 2007).

3.2 The Astigmatism of LUMM for Substance Addiction: The Myth of Global Autonomy Loss

The primary neuroethical astigmatism of LUMM as a treatment for substance addiction concerns the myth that individuals with addiction suffer a global loss of autonomy that renders them incapable of acting freely. Notwithstanding its popular appeal, this characterization of addiction seems to be false (Levy 2012). While addiction undoubtedly produces powerful desires, there is ample data to suggest that it is not strong enough to overwhelm individuals in the aforementioned manner. Strictly speaking, the strength of a particular desire can be measured by examining the behavior of individuals who are subject to it. It is precisely this test for strength that underlies the claim above: proponents of the global loss of autonomy conception argue their position by highlighting the lengths to which addicts will go in order to procure drugs. Addicts will engage, they suggest, in degrading and risky activities, including stealing and lying. Moreover, addicts will spend time and effort not only in pursuit of drugs, but also in attempts to stop consuming them. This latter endeavor indicates that, irrespective of what else is true of them, addicts genuinely desire (on many occasions) to refrain from acting on their addiction. However, though proponents of the global autonomy loss myth are correct to hold that behavioral evidence unmistakably indicates that addicts have impaired autonomy, addiction behaviors do not fit the profile expected when subject to irresistible desires. Individuals with the capacity for voluntary action who are subject to the irresistible desire to achieve a particular goal will pursue it across a broad range of circumstances, realistic and unrealistic alike. Hence, only a countervailing incentive that is itself of comparable power can limit or prevent the behavior (Levy 2012).

To be sure, the fact that an addict might refrain from using a drug in front of law enforcement personnel is not evidence of a resistible desire; however, were the addict to refrain for much smaller incentives – for instance, in order to spend money on food (while not at risk of starvation), or in order to schedule it for a more convenient time – this would mark resistible compulsion (Levy 2012). Contemporary evidence patently demonstrates that addictive behavior is sensitive to incentives that are not extraordinary in nature, and that it is not therefore subject to irresistible desires. Joanne Neale (2002) has highlighted the affect of price on drug quantity consumed by addicts, and

Herbert Fingarette (1988) reports that alcoholics exhibit sensitivity to cost even after a priming drink. Moreover, when a powerful reason to abstain is personally accepted and support is steadfastly provided throughout the withdrawal process, many addicts succeed in overcoming their addiction. New mothers, for instance, are frequently able to conquer their addiction in order to better care for their child. Gene Heyman (2009) has emphasized that addicts can be treated through the constructive of positive and negative behavioral incentives. Heyman draws heavily on the work of Stephen Higgins and colleagues (1994), who have successfully used rewards (in the form of vouchers) in the treatment of cocaine addiction. In a series of experiments, vouchers were paid to addicts in return for clear urine tests, with the value of each voucher increasing over time if the participant remained abstinent. The value of the vouchers did not exceed twelve dollars in United States currency, and was sometimes significantly lower than this figure. As Heyman notes, this is considerably less than the subjects were routinely spending on cocaine, yet the treatment modality was effective in encouraging the majority to abstain (Levy 2012).

The foregoing indications suggest that addicts are not subject to irresistible desires that entail a global loss of autonomy. Some evidence suggests that individuals with addiction may not be subject to desires to use drugs at all, at least on one understanding of the nature of desire, according to which human beings requisitely have positive attitudes toward desired objects (Levy 2012). Drugs may apparently be "wanted" – that is, they may possess a high incentive salience – without being "liked" at all (Robinson and Berridge 2003). David Balfour (2004) has identified the neural basis for this dissociation between the causal strength of a desire and the liking of its object as a consequence of the effects of dopamine on different regions of the NAc. One region is involved in the subjective feelings of reward associated with the drug while the other confers incentive salience on the stimulus independently of its being pleasurable. Heyman utilizes Balfour's study as a basis for claiming that addiction is a "disorder of choice" (Heyman 2009). By this phrase, he indicates that (i) addiction is a syndrome in which choice is disordered, but also that (ii) addiction is a syndrome in which dysfunctional behavior is chosen. At least *prima facie,* this conclusion seems to imply that individuals ought to treat addictive behaviors in the same way as other voluntary actions and hence to regard them as freely chosen and morally irresponsible, worthy of condemnation and punishment. Although Heyman's line of thought is alluring, this essay rejects it as acutely shortsighted. Autonomy manifests in degrees: it is not an all-or-nothing phenomenon. An individual may be capable of choice and suffer from diminished autonomy. While Heyman is technically correct to hold that addicts choose to act as they do, he fails to recognize

how severely impaired their autonomy to choose is. Addicts need not be in thrall to anyone else, but it is clear that they fail to adequately govern themselves. Addicts experience great difficulty in imposing their will on themselves, not in the manner that myth proponents imagine (i.e., because they feel forced to act, against their will, by overwhelming desires), but because although they may identify with their moment-to-moment choices, they cannot effectively pursue future plans and projects (Levy 2012).

Despite the fact that some individuals are more vulnerable to addiction than others (as suggested by the high heritability of substance abuse disorders), modern neuroscience has produced a substantial corpus of material on changes in the brain that together suggest that the discount curves of addicts alter as a consequence of the chronic use of addictive substances (Levy 2012). There is evidence that stimuli associated with substances to which an individual is addicted are highly motivating in ways that bypass capacities for conscious control. The motivational salience of a cue for the consumption of any good seems to be encoded as, or caused by, a surge in dopamine from the VTA. As individuals habituate toward a reward, this dopamine signal tends to attenuate. This attenuation fails to occur with regard to drugs of addiction, which may explain why their motivational salience increases even while the degree to which individuals prefer the drug tends to fall. Dopamine causes a heightened focus on predictors of reward and primes the motor system for action, leading to judgments that are difficult to revise and behavior that is difficult to inhibit. While these mechanisms cause judgments and behavior that would be strenuous for a well-functioning person to inhibit, addiction causes neuroadaptations that weaken the efficacy of the frontal mechanisms that regulate behavior. These neuroadaptations explain why addicts who sincerely wish to abstain from drug use nevertheless find it extremely difficult to prevent positive responses to drug-related cues. These neuroadaptations also explain the behavioral inconsistencies characteristic of addiction. Work in social psychology has demonstrated the existence of what may be a separate pathway whereby addicts find themselves oscillating between preferring abstention and preferring consumption (Baumeister 2002). Research on this phenomenon, known as "ego depletion," suggests that cognitive resources that individuals use to assess their options and inhibit prepotent responses are depletable. Utilizing these faculties leaves fewer available for subsequent self-control tasks and, hence, makes such tasks additionally cumbersome. In turn, ego depletion gives rise to the oscillation in preferences observed in addiction: when self-control resources are plentiful, the individual judges that abstention is best; when these resources are depleted, the individual experiences a judgment shift in favor of consumption (Levy 2012).

3.3. The Neuroethical Case Against LUMM: The Normative Demands of Proportionate Reason

For reasons beyond the unsavory implications of biomedicalization and the myth of global autonomy loss, this essay contends LUMM cannot be justified as a morally licit biomedical practice within the confines of a comprehensive normative ethical framework. The application of Richard McCormick's (1985) threefold criteria of proportionate reason can serve to illuminate the normative astigmatism of LUMM and the essay's corresponding endeavor to correct it. However, before an adequate moral assessment of an action's proportionality can be made, its effect on all ends and values must first be weighed. Moral values can be considered and a final decision made only after all values have been compared (Curran 1970). It is this systematic weighing of moral values, for instance, that has made noncombatant immunity a virtually exceptionless moral rule. The strength of moral norms touching concrete conduct is an elaboration of what is judged – within a particular culture, with a particular history, based on a particular experience – to be proportionate or disproportionate. Proportionality is always the criterion where actions cause damage, and neurocognitive memory manipulation involves both personal and social damage. The corrective vision provided herein attempts to halt the narrowly-conceived notion of proportionality embedded in the arguments of LUMM proponents (McCormick 1985).

If there exist norms that are teleologically established and yet are virtually exceptionless,[4] the remaining task is to clarify the metaethical assertions in view of which those norms are held as exceptionless. This task includes nondemonstrable calculations – prudential judgments based on the certainties of history and the uncertainties of the future. The sense of what individuals ought and ought not to do is therefore informed by past experience and agnosticism with regard to future behavior and its long-term effects. This suggests that where norms are viewed as virtually exceptionless, it is because of the prudential validity technically referred to as *lex lata in praesumptione periculi communis:* a law established on the presumption of common or universal danger (McCormick 1985). The notion of presumed universal danger is frequently associated with positive law. That is, even if the action in question does not threaten the individual personally (though LUMM does), there remains the further presumption that to allow individuals to make that decision for themselves poses a threat to the common good (which LUMM also does). Hence, the ethical impetus to retain autobiographically accurate, emotional rational, and narratively authentic memories can be viewed in a way analogous to the

4. For instance, the direct destruction of noncombatants in warfare.

exceptionless character of norms such as noncombatant immunity. The risk in alternative policies is simply too great. In the context of moral development, autobiographical, emotional, and narrative memories are enormous goods at stake. Past experience of human failure, inconsistency, and frailty, along with uncertainty regarding long-term effects of such irreversible actions as dampening or erasing human memories, suggests that societies should continue to hold some norms - such as authentic self-knowledge – as virtually exceptionless. That is the conclusion of prudence in the face of dangers too grave to make risk tolerable.

For McCormick, proportionate reason (for permitting the occurrence of harm otherwise judged as illicit within a normative moral calculus) means three things: (i) the value at stake is at least equal to the value being sacrificed; (ii) there is no less harmful way to protect the value here and now; and (iii) the means used to protect the value (here and now) will not undermine it in the long run (McCormick 1985). Conversely, an action is disproportionate if (i) a lesser value is preferred to a more important one; (ii) harm is unnecessarily caused in the protection of a greater good; or (iii) in the circumstances, the manner of protecting the good will undermine it in the long run. To determine if an action involving harm is proportionate in the circumstances, one must judge whether the specific choice is the best possible service to all values in the difficult and, in the context of PTSD and substance addiction, tragic circumstances. What constitutes the best promotion of all values in the circumstances will, of course, depend on how one defines and understands the circumstances. An adequate account of the circumstances indicates not simply how much quantitative good can be salvaged from an individual conflict of values, but also the weight and balance of social implications and reverberating aftereffects insofar as they can be foreseen. This account will test generalizability, consider cultural climate, draw from historical wisdom, seek guidance from others, and distance itself from self-interested tendencies. In sum, the criterion of proportionality is found within the *ordo bonorum,* which determines the good one ought to do and serves as the objectively licit character of one's activity. So informed and organized, individuals do all that can be expected of them (McCormick 1985).

Before applying McCormick's first criterion of proportionality – namely, that the value at stake is at least equal to the value being sacrificed – to the action of LUMM (McCormick 1985), it is necessary, first, to identify both the value at stake and the value being sacrificed in the circumstances of LUMM. The strongest proponents of LUMM are likely to define the value at stake as individual (and, in turn, social) health, well-being, and safety (which has been compromised by disproportionate psychosocial conditions including, but not limited to, PTSD and substance addiction). This essay defines the

value being sacrificed as individual (and social) autobiographical memory, emotional rationality, and narrative identity – elements that together comprise the ability to seek, identify, and act on the good. There is no doubt that individual (and social) health, well-being, and safety are massively significant values. However, as LUMM proponents fail to discern, these values depend almost exclusively for existence on some manifestation of the interplay between memory, emotion, and identity. If overall health, well-being, and safety are largely contingent on the capacities to understand (employing memory), evaluate (employing emotion), and reason (employing identity), then LUMM does not meet McCormick's first criterion of proportionality. Indeed, the value at stake is not equal to the value being scarified.

McCormick's second criterion of proportionality requires that there exists no less harmful way to protect the value here and now (McCormick 1985). Applied in the context of LUMM, the criterion becomes thus: there exists no less harmful way to protect the value of individual (and social) health, well-being, and safety than to annihilate the memories that are presumed to be responsible for perpetuating disproportionate psychosocial conditions (including, but not limited to, PTSD and substance addiction). This claim is an enormous stretch, even in light of most aggressive and debilitating psychosocial conditions. Moreover, it is based on the false premises that (i) memories are solely or even primarily responsible for perpetuating psychosocial conditions, and (ii) memories are independently and immutably morally charged. Neither of these claims carry any neurobiological or neuroethical merit. Lastly, if the value being scarified is defined as individual (and social) autobiographical memory, emotional rationality, and narrative identity – elements that, again, collectively comprise the ability to seek, identify, and act on the good – then it is difficult to imagine a more harmful way protect the value here and now than to utilize LUMM to do so. In light of the abilities of intensive psychotherapy and the proportionate use of rebalancing pharmacologicals (when utilized to their fullest potential),[5] LUMM does not meet McCormick's second criterion of proportionality. Indeed, there exists a drastically less harmful (and impermanent) way to protect the value here and now.

McCormick's third criterion of proportionality requires that in the circumstances, the means used to protect the value here and now will not undermine it in the long run (McCormick 1985). Applied in the context of LUMM, the criterion becomes thus: in the circumstances of threatening psychosocial conditions, the means of LUMM used

5. This oversimplified statement is meant to include participation by those with addiction in the many historically-successful 12-step recovery programs.

(here and now) to protect the value of individual (and social) health, well-being, and safety will not undermine it (i.e., individual [and social] health, well-being, and safety) in the long run. Here, the neuroethical astigmatism of LUMM proponents is most acutely evident. Proponents of LUMM frequently couch their arguments in what they believe would result from the redemptive practice of LUMM: the restoration and reinstallation of autonomy once plundered by debilitating and disproportionate psychosocial conditions. By itself, the restoration and reinstallation of autonomy is a noble and desirable goal for any treatment. As mentioned above, if the consequence of certain psychosocial conditions involves the loss of autonomy, then the conditions(s) must be viewed to somehow undercut the individual (and social) ability to pursue goals. This presumes, however, that the pursuit of individual (and social) goals – which depends for existence on the capacities to (i) recall (through memory) and (ii) act (through informed and intentioned will) on them – will somehow be resurrected by annihilating the very faculty (i.e., memory) that makes the pursuit possible and, more importantly, morally responsible. However, goals are always specific; they cannot exist apart from individuals and societies who espouse them, and they depend for definition, therefore, on the characteristics those individuals and societies possess – characteristics that are, no doubt, very different from other individuals and societies.

A standard understanding of autonomy refers to the freedom individuals (and societies) ought to enjoy to choose their own way in life and to make their own decisions within moral limits. Proponents of LUMM contend there is no more immediate and humane way, in extreme circumstances, to restore and reinstate lost freedom than to dampen or erase the memories that seem to imprison it. For them, LUMM marks a bridge for individuals (and societies) bound by the devastating effects of psychosocial disorders to once again be free to act freely. A first blush, this position is tempting and intoxicating, but it ultimately proves astigmatic and impossible. Societies have long nuanced the notion of pure autonomy to preclude the freedom of its members to simply do as they wish. This is exemplified in the rejection, for instance, of strictly utilitarian calculi and purely consequentialist logistics. Against the notion of pure autonomy, this essay suggests that a more adequate understanding of autonomy is not fundamentally concerned with the freedom to do as one wants, but with the freedom to do as one ought in light of one's moral responsibilities.

If this nuanced notion of autonomy is persuasive, then it raises the question of how individuals can decipher what they have a moral responsibility to do. As the central thesis of this essay holds, the answer is determined by one's narrative identity, the sum of one's autobiographical memory and emotional rationality. The "autonomous ought"

can therefore exist only in light of an idiosyncratic narrative. Hence, only within an idiosyncratic narrative structure can one determine one's future "oughtness" – the pull of moral responsibility grounded in and determined by the story of one's life and the values and commitments that comprise it. Conceived of concretely, the "autonomous ought" is what separates an individual's lack of desire to help the child in front of her from the responsibility to help the child in front of her because this child is her child and she is this child's parent. This structure of identity, which serves as the basis for determining the good and one's responsibility to act on it, is irreparably damaged by memory manipulation, even in its most limited forms and exceptional applications. For this reason, LUMM does not meet McCormick's third criterion of proportionality. Indeed, in the circumstances, the means used (here and now) to protect the value ultimately undermine it in the long run.

Conclusion

This essay has offered a critical response to proponents of LUMM. Part 1 examined LUMM for PTSD, and included a specific analysis of the neurobiology of PTSD and beta-adrenergic receptor-blocking pharmacologicals as treatment for the disorder. It concluded by identifying the strongest possible case in favor of LUMM for PTSD. Part 2 explored LUMM for substance addition, and included a specific analysis of the neurobiology of substance addiction and DBS and FMC as treatments for the disease. It concluded by proffering the strongest possible case in favor of LUMM for substance addiction. Finally, Part 3 evaluated the neuroethical astigmatism of LUMM, and included a specific analysis of biomedicalization and the codification of new diseases, as well as the myth of global autonomy loss. It concluded by proposing that LUMM violates the normative demands of proportionate reason.

The evidence provided in this essay supports the conclusion that interventions to dampen, disassociate, erase, and replace episodic memories of trauma and addiction ultimately undermine one's ability to seek, identify, and act on the good. As such, memory manipulation, even in its most limited forms, cannot be ethically justified as a licit medical practice.

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